DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
1401 Rockville Pike
Rockville MD 20852-1448

June 19, 1998

Our Reference No.: 97-1359

Mr. Bogdan Dziurzynski
MedImmune, Inc.
35 West Watkins Mill Road
Gaithersburg, MD 20878

Dear Mr. Dziurzynski:

This letter hereby issues Department of Health and Human Services Biologics License No. 1252 to MedImmune, Inc., Gaithersburg, Maryland, in accordance with the provisions of Title III Part F of the Public Health Service Act, as amended November 21, 1997 (FDAMA; Public Law 105-115), controlling the manufacture and sale of biological products. This license authorizes you to manufacture and ship for sale, barter, or exchange, in interstate and foreign commerce, those products for which your company has demonstrated compliance with establishment and product standards.

Under this license you are authorized to manufacture the product Palivizumab. Palivizumab is to be used for prophylaxis of serious lower respiratory tract disease, caused by respiratory syncytial virus, in pediatric patients at high risk of RSV disease.

Under this authorization, you are approved to manufacture Palivizumab at your facility in Gaithersburg, Maryland. Final formulated drug product will be filled, lyophilized, labeled, and packaged a[redacted], and distributed from [redacted] In accordance with approved labeling, your product will bear the tradename Synagis, and will be marketed in single use vials containing 100 mg of Palivizumab.

You are not currently required to submit samples of future lots of Palivizumab to the Center for Biologics Evaluation and Research (CBER) for release by the Director, CBER, under 21 CFR 610.2. FDA will continue to monitor compliance with 21 CFR 610.1 requiring assay and release of only those lots that meet release specifications.

The dating period for Palivizumab shall be 18 months from the date of manufacture when stored at 2-8°C. The date of manufacture shall be defined as the date of final sterile filtration of the final formulated product. The drug substance may be stored for up to 6 months at 2-8°C. Results of ongoing stability studies should be submitted throughout the dating period as they become available including the results of stability studies from the first three production lots. The stability protocol in your license application is considered approved for the purpose of extending the expiration dating period of your drug substance and drug product as specified in 21 CFR 601.12.

Any changes in the manufacturing, testing, packaging or labeling of Palivizumab, or in the manufacturing facilities will require the submission of information to your biologics license application for our review and written approval consistent with 21 CFR 601.12.

We acknowledge your written commitments specified in your letter of June 18, 1998, which include the following:

1. To design and conduct a monitoring program to evaluate specimens obtained from RSV hospitalized patients to assess RSV neutralization. The data from the program will be reported annually to FDA and at the conclusion of three years monitoring, MedImmune, Inc. will consult with FDA to determined whether the frequency of monitoring may be adjusted.

2. To design in collaboration with FDA and conduct a safety study in pediatric congenital heart disease patients.

3. To provide a final report of [redacted] (second year prophylaxis safety study) by July 1, 1998.

4. To provide additional manufacturing information:

   a. To complete column use studies with used gels at the end of column lifetime. To continue specified impurity testing as part of lot release until the results of these studies support control through process validation.

   b. To submit the protocol and summary results for column cleaning effectiveness studies at laboratory and manufacturing scales by September 30, 1998.

   c. To submit the protocol and summary results for hold period studies for in-process product and buffers by September 30, 1998.

d. To complete shipping validation studies by August 31, 1998. In the interim period it is understood that you will utilize a temperature monitoring and recording device in each shipment to assure that required shipping temperatures were maintained.

e. To submit the protocol and summary results for studies to verify that ——— ——————————— does not mask the detection of mycoplasma or other microorganisms in tests for sterility by September 30, 1998.

f. To submit the protocol and summary results for studies to demonstrate clearance of ——————— by the drug substance purification process by September 30, 1998.

g. To submit the protocol and summary results for the validation of the improved ——————————— assay by September 30, 1998.

h. To submit a revised validation protocol for anticipated lyophilizer load sizes by July 15, 1998 and a summary report of the first three lots evaluated under that protocol within 30 days following completion of data analysis.

5. We also acknowledge additional information in your letter of June 18, 1998 addressing the agency's observations noted during the March 26 - April 6, 1998 prelicense inspection and your commitment to submit additional information and data within the timelines specified.

It is requested that adverse experience reports be submitted in accordance with the adverse experience reporting requirements for licensed biological products (21 CFR 600.80) and that distribution reports be submitted as described (21 CFR 600.81). All adverse experience reports should be prominently identified according to 21 CFR 600.80 and be submitted to the Center for Biologics Evaluation and Research, HFM-210, Food and Drug Administration, 1401 Rockville Pike, Rockville, MD 20852-1448.

Please submit three copies of all final printed labeling at the time of use and include part II of the label transmittal form (FDA Form 2567) with completed implementation information. In addition, you may wish to submit draft copies of the proposed introductory advertising and promotional labeling with an FDA form 2567 to the Center for Biologics Evaluation and Research, Advertising and Promotional Labeling Staff, HFM-202, 1401 Rockville Pike, Rockville, MD 20852-1448. Final printed advertising and promotional labeling should be submitted at the time of initial dissemination, accompanied by an FDA Form 2567.

All promotional claims must be consistent with and not contrary to approved labeling. No comparative promotional claim or claim of superiority over other products should be made unless data to support such claims are submitted to and approved by the Center for Biologics Evaluation and Research.

Please acknowledge receipt of the enclosed biologics license to the Director, Division of Application Review and Policy (HFM-585), Center for Biologics Evaluation and Research.

Sincerely yours,

Shawn A Riso

for Jay P. Siegel, M.D., FACP
Director
Office of Therapeutics
Research and Review
Center for Biologics
Evaluation and Research

Enclosure